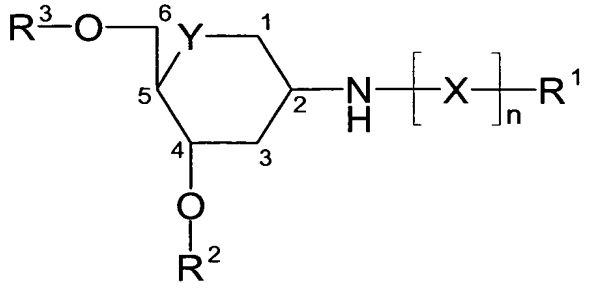
Patent Claims

1. A compound of the formula I,

(Formula I)



wherein Y is selected from the group consisting of O, S, and NR^4, whereby R^4 is alkyl-, alkenyl, alkinyl, aryl-, acyl-, a protecting group or H,

wherein X is a linking moiety whereby n is 0 or 1,

wherein R^1 is independent from R^2, R^3 and R^4, and wherein R^1 is selected from the group consisting of

(1) a protecting group,
(2) a label, and
(3) a solid phase,

wherein R^2 and R^3 are independent from each other and independent from R^1 or R^4, and wherein R^2 and R^3 are selected from the group consisting of

(1) –H,
(2) a protecting group,
(3) a solid phase and a linking moiety X,
(4) a phosphoramidite,
(5) a H-phosphonate, and
(6) a triphosphate,

with the proviso that R^3 but not R^2 can be triphosphate and R^1 is not a solid phase if R^3 is a triphosphate,

with the proviso that R^2 and R^3 are not both a solid phase, not both a phosphoramidite, not both a H-phosphonate, not both -H or not both a protecting group, or not a phosphoramidite and a H-phosphonate, or not a

solid phase and a phosphoramidite, or not a solid phase and a H-phosphonate,

and with the proviso that when one residue selected from the group consisting of R^1, R^2 or R^3 is a solid phase then the other two residues selected from the group consisting of R^1, R^2 or R^3 are not a solid phase.

2. A compound according to claim 1,
characterised in that
the linking moiety X comprises carbon and oxygen atoms.

3. A compound according to any of the claims 1 or 2,
characterised in that
the linking moiety X comprises $-(CH_2)_m$ or $-(CH_2CH_2O)_m$ moieties,
whereby m is an integer number between 1 and 10.

4. A compound according to any of the claims 1 to 3,
characterised in that
the linking moiety X is selected from the group consisting of
(1) $-CO-(CH_2)_m-Z-$
(2) $-CO-(CH_2CH_2O)_m-CH_2CH_2-Z-$
whereby m is an integer number between 0 and 10 and
whereby Z is selected from the group consisting of NH, CO, O and S.

5. A compound according to claim 4,
characterised in that
Y is O.

6. A compound according to any of the claims 1 to 5,
characterised in that
the protecting group is selected from the group consisting of

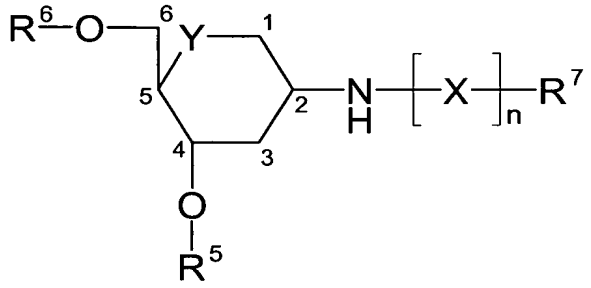
(1) fluorenylmethoxycarbonyl-,
(2) dimethoxytrityl-,
(3) monomethoxytrityl-,

(4) trifluoroacetyl-,
(5) levulinyl-, and
(6) silyl-.

7. A compound according to any of the claims 1 to 6,
characterised in that,
the label is selected from the group consisting of
(1) a fluorescein dye,
(2) a rhodamine dye,
(3) a cyanine dye, and
(4) a coumarin dye.

8. A compound according to any of the claims 1 to 7,
characterised in that
the compound is a derivative of
1,5-anhydro-2-amino-2,3-dideoxy-D-mannitol or
1,5-anhydro-2-amino-2,3-dideoxy-D-glucitol.

9. An oligomeric compound comprising a monomeric unit with formula II:



(formula II)

wherein Y is selected from the group consisting of O, S and NR^4,
whereby R^4 is alkyl-, alkenyl, alkinyl, aryl-, acyl-, a protecting group or H;

wherein X is a linking moiety whereby n is 0 or 1;

wherein R^7 is independent from R^4, R^5 and R^6 and wherein R^7 is selected from the group consisting of

(1) –H,

(2) a protecting group,

(3) a label,

(4) an oligonucleotide, and

(5) a solid phase,

wherein R^5 and R^6 are independent from each other and independent from R^4 or R^7,

and wherein R^5 and R^6 are selected from the group consisting of

(1) –H,

(2) a solid phase and a linking moiety X,

(3) a phosphate, and

(4) a phosphodiester with a nucleotide, a modified nucleotide, an oligonucleotide or a modified oligonucleotide,

with the proviso that R^5 and R^6 are not both –H, both a solid phase and a linking moiety X, both a phosphate, or –H and a phosphate,

with the proviso that when one residue selected from the group consisting of R^5, R^6 or R^7 is a solid phase then the other residues selected from the group consisting of R^5, R^6 or R^7 are not a solid phase.

10. The oligomeric compound according to claim 9,
characterised in that
the linking moiety X comprises carbon and oxygen atoms.

11. The oligomeric compound according to any of the claims 9 to 10,
characterised in that
the linking moiety X comprises $-(CH_2)_m$ or $-(CH_2CH_2O)_m$ moieties
whereby m is an integer number between 1 and 10.

12. The oligomeric compound according to any of the claims 9 to 11,
characterised in that
the linking moiety X is selected from the group consisting of

(1) $-CO-(CH_2)_m-Z-$

(2) $-CO-(CH_2CH_2O)_m-CH_2CH_2-Z-$

whereby m is an integer number between 0 and 10 and
whereby Z is selected from the group consisting of NH, CO, O and S.

13. The oligomeric compound according to claim 12,
characterised in that
Z is NH and Y is O.

14. The oligomeric compound according to any of the claims 9 to 13,
characterised in that
the protecting group is selected from the group consisting of
(1) fluorenylmethoxycarbonyl-,
(2) dimethoxytrityl-,
(3) monomethoxytrityl-,
(4) trifluoroacetyl-,
(5) levulinyl-, or
(6) silyl-.

15. The oligomeric compound according to any of the claims 9 to 14,
characterised in that the label is a fluorescent label.

16. The oligomeric compound according to any of the claims 9 to 15,
characterised in that
the modified oligonucleotide comprises a monomeric unit that is
(1) a linking moiety with a second label attached to a nucleotide, or
(2) a linking moiety with a second label attached to a modified nucleotide or a non-nucleotide compound.

17. The oligomeric compound according to claim 16,
characterised in that
the second label is a second fluorescent label.

18. The oligomeric compound according to any of the claims 15 to 17,
characterised in that,

the fluorescent label or the second fluorescent label is selected from the group consisting of

(1) a fluorescein dye,
(2) a rhodamine dye,
(3) a cyanine dye, and
(4) a coumarin dye.

19. The oligomeric compound according to any of the claims 9 to 18, characterised in that
the oligomeric compound cannot be extended enzymatically.

20. The oligomeric compound according to claim 19,
characterised in that
the monomeric unit at the 3'-end of the oligomeric compound is
- a 2',3'-dideoxy-nucleotide or
- a 3'-phosphorylated nucleotide.

21. Use of a compound according to any of the claims 1 to 8, wherein R^2 is a phosphoramidite or a solid phase with a linking moiety X and R^3 is a protecting group, for the chemical synthesis of an oligomeric compound according to any of the claims 9 to 20.

22. Use of an oligomeric compound according to any of the claims 9 to 20 in a hybridisation reaction with a nucleic acid.

23. Use of an oligomeric compound according to any of the claims 9 to 20 as a primer, probe or capture probe.

24. A method for the chemical synthesis of an oligomeric compound according to any of the claims 9 to 20,
comprising the steps of

(a) providing a compound according to any of the claims 1 to 8, wherein R^2 is phosphoramidite and R^3 is a protecting group,
(b) providing a 5'-OH group of a nucleoside or a modified nucleoside bound to a solid phase by the 3'-OH group, or

providing a 5'-OH group of an oligonucleotide or a modified oligonucleotide bound to a solid phase by the 3'-OH group of the nucleotide or the modified nucleotide at the 3'end of the oligonucleotide or the modified oligonucleotide,

(c) reacting the phosphorous atom of the phosphoramidite with the 5'-OH group to form a phosphite ester and oxidizing the phosphite ester to a phosphotriester,

(d) optionally reacting any unreacted 5'-OH group of step (c) with another compound to prevent any further reactions of the unreacted 5'-OH group of step (c) in the following steps,

(e) optionally repeating steps (a) to (d) with phosphoramidite derivatives of nucleosides or modified nucleosides after removal of the protecting group of the compound according to any of the claims 1 to 8, and

(f) cleaving the oligomeric compound from the solid phase, removing the protecting groups and thereby converting the phosphotriester to a phosphodiester, and

(g) isolating the oligomeric compound.

25. A method for the enzymatic synthesis of a polymeric compound or an oligomeric compound according to any of the claims 9 to 20 comprising the steps of

(a) incubating a compound according to any of the claims 1 to 8, wherein R^3 of said compound is a triphosphate, with a 3'-OH group of the nucleotide or modified nucleotide at the 3'-end of a polynucleotide, oligonucleotide or a modified oligonucleotide in the presence of terminal transferase, whereby the compound is attached to the 3'-OH, whereby pyrophosphate is released, and

(b) isolating the polymeric or oligomeric compound.

26. A method to attach a label to an oligomeric compound according to any of the claims 9 to 20, whereby R^7 of the oligomeric compound is a protecting group, comprising the steps of

(a) removing the protecting group R^7, and

(b) reacting the deprotected moiety of the oligomeric compound with the label.

27. A method for the detection of a target nucleic acid in a sample comprising the steps of

(a) providing a sample suspected to contain the target nucleic acid

(b) providing an oligomeric compound according to any of the claims 9 to 20, which is essentially complementary to a part or all of the target nucleic acid,

(c) optionally amplifying the target nucleic acid with a template-dependent DNA polymerase and primers

(d) contacting the sample with the oligomeric compound under conditions for binding the oligomeric compound to the target nucleic acid,

(e) determining the binding product or the degree of hybridization between the target nucleic acid and the oligomeric compound as a measure of the presence, absence or amount of the target nucleic acid.

28. The method according to claim 27, wherein the oligomeric compound is an oligomeric compound according to any of the claims 15 to 20.

29. The method according to any of the claims 27 to 28, whereby in step (d) the degree of hybridization is determined by the quantity of the first or second fluorescent label that is released from the oligomeric compound hybridized to the target nucleic acid by exonuclease hydrolysis by the template-dependent DNA polymerase.

30. A method for detecting the presence or absence of a target nucleic acid in a sample, comprising the steps of:
performing at least one cycling step, wherein a cycling step comprises an amplifying step and a hybridizing step, wherein said amplifying step comprises contacting said sample with primers to produce a an amplification product if target nucleic acid is present in said sample, wherein said hybridizing step comprises contacting said sample with a pair of probes, wherein at least one of the probes is an oligomeric compound according to any of the claims 9 to 20 wherein R^7 is a label, wherein the members of said

pair of probes hybridize to said amplification product within no more than five nucleotides of each other, wherein a first probe of said pair of probes is labeled with a donor fluorescent label and wherein a second probe of said pair of probes is labeled with a corresponding acceptor fluorescent label;
and detecting the presence or absence of fluorescence resonance energy transfer between said donor fluorescent label of said first probe and said acceptor fluorescent label of said second probe, wherein the presence of fluorescence resonance energy transfer is indicative of the presence of the target nucleic acid in the sample, and wherein the absence of fluorescence resonance energy transfer is indicative of the absence of the target nucleic acid in the sample.

31. Kit of parts containing
- a template-dependent polymerase having 3' to 5' exonucleolytic activity,
- a set of primers,
- nucleotides, and
- an oligomeric compound according to any of the claims 9 to 20, wherein R^7 is a label.